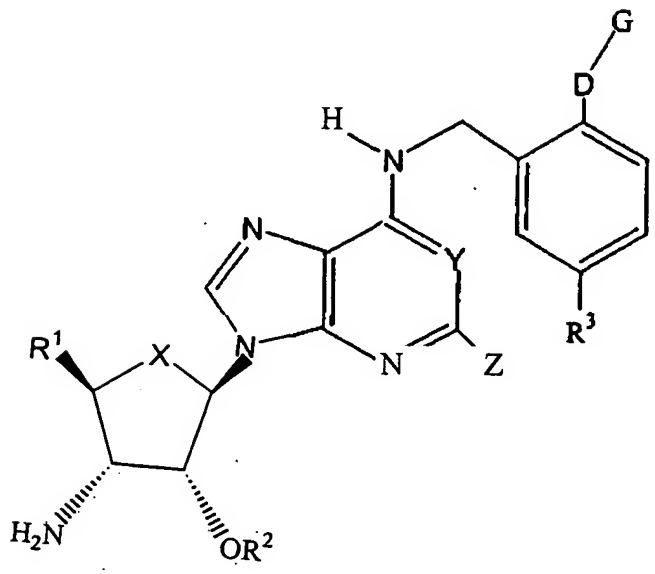
IN THE CLAIMS:

1. (Original): A compound of the formula I



Formula I

a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug, wherein X is oxy, methylene or thio; Y is CH or N; Z is H, (C_1-C_4)alkyl, (C_1-C_4)alkyloxy, trifluoromethyl or halo; R^1 is hydroxymethyl, (C_1-C_3)alkoxymethyl, (C_3-C_5)cycloalkoxymethyl, carboxy, (C_1-C_3)alkoxycarbonyl, (C_3-C_5)cycloalkoxycarbonyl, 1,1-aminoiminomethyl, 1,1-(mono-N- or di-N,N-(C_1-C_4)alkylamino)iminomethyl, 1,1-(mono-N- or di-N,N-(C_3-C_5)cycloalkylamino)iminomethyl, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminocarbonyl or N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylaminocarbonyl; R^2 is H, (C_1-C_3)alkyl or (C_3-C_5)cycloalkyl; R^3 is halo, trifluoromethyl, cyano, (C_1-C_3)alkyl, (C_1-C_3)lkyloxy, ethenyl or ethynyl; D

is oxy, thio, NH, $(C_1\text{-}C_6)$alkyloxy, $(C_1\text{-}C_6)$alkylthio or $(C_1\text{-}C_6)$alkylamino; G is a partially saturated, fully saturated or fully unsaturated five to eight membered ring optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen; wherein said G is optionally mono-, di- or tri-substituted independently with halo, $(C_1\text{-}C_3)$alkyl, trifluoromethyl, trifluoromethoxy, nitro, cyano, $(C_3\text{-}C_5)$cycloalkyl, hydroxy or $(C_1\text{-}C_3)$alkoxy or G is cyano, $(C_1\text{-}C_4)$alkoxycarbonyl, $(C_3\text{-}C_5)$cycloalkoxycarbonyl, $C(O)NR^4R^5$, $C(S)NR^4R^5$, $C(NH)NR^4R^5$, $C(N(C_1\text{-}C_3)\text{alkyl})NR^4R^5$ or $C(N(C_3\text{-}C_{10})\text{cycloalkyl})NR^4R^5$; R^4 is a bond, H, $(C_1\text{-}C_{10})$alkyl, hydroxy, $(C_1\text{-}C_{10})$alkoxy, $(C_3\text{-}C_{10})$cycloalkoxy or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through $(C_1\text{-}C_3)$alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring or a bicyclic ring with optional $(C_1\text{-}C_3)$bridge optionally linked through $(C_1\text{-}C_3)$alkyl, said bicyclic ring or bridged bicyclic ring optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen wherein said $(C_1\text{-}C_{10})$alkyl, $(C_1\text{-}C_{10})$alkoxy, $(C_3\text{-}C_{10})$cycloalkoxy or R^4 ring(s) is optionally mono-, di- or tri-substituted independently with halo, $(C_1\text{-}C_3)$alkyl, trifluoromethyl, nitro, cyano, $(C_3\text{-}C_5)$cycloalkyl, hydroxy or $(C_1\text{-}C_3)$alkoxy; R^5 is a bond, H, $(C_1\text{-}C_{10})$alkyl or $(C_1\text{-}C_{10})$cycloalkyl; or R^4 and R^5 taken together with the nitrogen to which they are attached form a fully saturated or partially unsaturated four to nine membered ring, said ring optionally bridged, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, said ring optionally mono- or di-substituted independently with oxo, hydroxy, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_8)$alkyl, amino, mono-N- or di-N,N-$(C_1\text{-}$

C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminocarbonyl, N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, mono-N- or di-N,N-(C_3-C_5)cycloalkylamin, N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylamino, formylamino, (C_1-C_4)alkylcarbonylamino, (C_3-C_5)cycloalkylcarbonylamino, (C_1-C_4)alkoxycarbonylamino, N-(C_1-C_4)alkoxycarbonyl-N-(C_1-C_4)alkylamino, (C_1-C_4)sulfamoyl, (C_1-C_4)alkylsulfonylamino, (C_3-C_5)cycloalkylsulfonylamino or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally linked through (C_1-C_3)alkyl, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen, and optionally mono- or di-substituted with halo, trifluoromethyl, trifluoromethoxy, (C_1-C_3)alkyl or (C_1-C_3)alkoxy.

2. (Original): A compound as recited in claim 1 wherein X is oxy; Y is N; Z is H; R^1 is (C_1-C_6)alkylcarbamoyl; R^2 is H; R^3 is halo, trifluoromethyl, cyano, (C_1-C_3)alkyl, (C_1-C_3)alkyloxy, ethenyl or ethynyl; D is oxy, thio, (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is phenyl, pyridyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, isoxazolyl, pyridinazinyl, tetrazolyl, isothiazolyl, thiophenyl, furanyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyrazolyl, pyrrolyl, indolyl, naphthalenyl, quinolinyl, isoquinolinyl, benzo[b]furanyl, benzo[b]thiophenyl, benzothiazolyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, morpholinyl wherein said G is optionally mono-, di- or tri-substituted independently with halo, (d-C_3)alkyl or (d-C_3)alkoxy, or a pharmaceutically acceptable salt thereof.

3. (Original): A compound as recited in claim 2 wherein R^1 is methylcarbamoyl; R^3 is halo; D is $(C_1$-$C_6)$alkoxy; G is phenyl, pyridyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, furanyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyrazolyl, pyrrolyl wherein said G is optionally mono-, di- or tri-substituted independently with halo, $(C_1$-$C_3)$alkyl, trifluoromethoxy or $(C_1$-$C_3)$alkoxy, or a pharmaceutically acceptable salt thereof.

4. (Original): A compound as recited in claim 3 wherein D is $(C_1$-$C_2)$alkoxy; G is phenyl, thiazolyl, oxazolyl, isoxazolyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl or morpholinyl wherein said G is optionally mono-, di- or tri-substituted independently with halo, $(C_1$-$C_3)$alkyl or $(C_1$-$C_3)$alkoxy, or a pharmaceutically acceptable salt thereof.

5. (Original): A compound as recited in claim 3 wherein R^3 is chloro; D is methyleneoxy; and G is phenyl, or a pharmaceutically acceptable salt thereof.

6. (Original): A compound as recited in claim 3 wherein R^3 is chloro; D is methyleneoxy; and G is 3-furanyl, or a pharmaceutically acceptable salt thereof.

7. (Original): A compound as recited in claim 3 wherein R^3 is chloro; D is methyleneoxy; and G is 2-furanyl, or a pharmaceutically acceptable salt thereof.

8. (Original): A compound as recited in claim 3 wherein R^3 is chloro; D is methyleneoxy; and G is 2-thiazolyl, or a pharmaceutically acceptable salt thereof.

9. (Original): A compound as recited in claim 3 wherein R^3 is chloro; D is methyleneoxy; and G is 5-(3-methylisoxazolyl), or a pharmaceutically acceptable salt thereof.

10. (Original): A compound as recited in claim 1 wherein X is oxy; Y is N; Z is H; R^1 is (C_1-C_6)alkylcarbamoyl; R^2 is H; R^3 is halo, trifluoromethyl, cyano, (C_1-C_3)alkyl, (C_1-C_3)alkyloxy, ethenyl or ethynyl; D is (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is $C(O)NR^4R^5$or$C(S)NR^4R^5$ wherein R^4 and R^5 taken together with the nitrogen to which they are attached form a fully saturated four to nine membered ring, optionally having one to three additional heteroatoms selected independently from oxygen, sulfur and nitrogen, said ring optionally mono- or di-substituted independently with oxo, (C_1-C_6)alkoxy, (C_1-C_8)alkyl, amino, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminocarbonyl, N-(C_1-C_4)alkyl-N-(C_3-C_s)cycloalkylaminocarbonyl, mono-N- or di-N,N-(d-C_4)alkylamino, mono-N- or di-N,N-(C_3-C_5)cycloalkylamino or N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylamino, formylamino, (C_1-C_4)alkylformylamino, (C_3-C_5)cycloalkylformylamino, sulfamoyl, (Crd)alkylsulfonylamino, (C_3-C_5)cycloalkylsulfonylamino or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alky'l, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally linked through (C_1-C_3)alkyl, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen, or a pharmaceutically acceptable salt thereof.

11. (Original): A compound as recited in claim 10 wherein R^1 is methylcarbamoyl; R^3 is halo; D is (C_1-C_2)alkoxy; G is $C(O)NR^4R^5$or $C(S)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl, piperazinyl, morpholinyl, azetidinyl or pyrrolidinyl said ring optionally mono- or di-substituted independently with oxo, hydroxy, (C_1-C_6)alkoxy, (C_1-C_8)alkyl, amino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminocarbonyl, N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, mono-N- or di-N,N-(C_3-C_5)cycloalkylamino or N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylamino, formylamino, $(Ci-C_4)$alkylformylamino, (C_3-C_5)cycloalkylformylamino, sulfamoyl, (C_1-C_4)alkylsulfonylamino, (C_3-C_5)cycloalkylsulfonylamino or a partially saturated, fully saturated or fully unsaturated four to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen, or a pharmaceutically acceptable salt thereof.

12. (Original): A compound as recited in claim 11 wherein G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl, piperazinyl, morpholinyl, azetidinyl, pyrrolidinyl said ring optionally mono- or di-substituted independently with hydroxy, oxo,(C_1-C_6)alkoxy, (C_1C_8)alkyl, amino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, or a partially saturated, fully saturated or fully unsaturated four to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen, or a pharmaceutically acceptable salt thereof.

13 (Original): A compound as recited in claim 12 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperazinyl substituted in the four position with methyl, or a pharmaceutically acceptable salt thereof.

14. (Original): A compound as recited in claim 12 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperazinyl, or a pharmaceutically acceptable salt thereof.

15. (Original): A compound as recited in claim 12 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; wherein R^4 and Retaken together with the nitrogen to which they are attached form piperidinyl substituted in the four position with N,N-dimethylamino, or a pharmaceutically acceptable salt thereof.

16. (Original): A compound as recited in claim 12 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl substituted in the four position with piperidin-1-yl, or a pharmaceutically acceptable salt thereof.

17. (Original): A compound as recited in claim 12 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl substituted in the four position with methylamino, or a pharmaceutically acceptable salt thereof.

18. (Original): A compound as recited in claim 1 wherein X is oxy; Y is N; Z is H; R^1 is (C_1-C_6)alkylcarbamoyl; R^2 is H; R^3 is halo, trifluoromethyl, cyano, (C_1-C_3)alkyl, (C_1-C_3)alkyloxy, ethenyl or ethynyl; D is (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is $C(O)NR^4R^5$ or $C(S)NR^4R^5$ R^4 is H, (C_1-C_{10})alkyl, hydroxy, (C_1-Cio)alkoxy, (C_3-C_{10})cycloalkoxy or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally linked through (C_1-C_3)alkyl, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen; R^5 is H, (C_1C_{10})alkyl or (C_1-C_{10})cycloalkyl, or a pharmaceutically acceptable salt thereof.

19. (Original): A compound as recited in claim 18 wherein R^1 is methylcarbamoyl; R^3 is halo; D is (C_1-C_2)alkoxy; G is $C(O)NR^4R^5$ or $C(S)NR^4R^5$; R^4 is H, (C_1-C_{10})alkyl hydroxy, (C_1-C_{10})alkoxy, (C_3-C_{10})cycloalkoxy or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen; and R^5 is H, (C_1-C_{10})alkyl or (C_1-C_{10})cycloalkyl, or a pharmaceutically acceptable salt thereof.

20. (Original): A compound as recited in claim 19 wherein G is $C(O)NR^4R^5$ R^4 is H, (C_1-C_{10})alkyl, (C_3-C_6)cycloalkyl, hydroxy, (C_1-C_{10})alkoxy or (C_3-C_{10})cycloalkoxy; and R^5 is H, (C_1-C_{10})alkyl or (C_3-C_{10})cycloalkyl, or a pharmaceutically acceptable salt thereof.

21. (Original): A compound as recited in claim 20 wherein R^3 is chloro; D is methyleneoxy; G is $C(O)NR^4R^5$; R^4 is H; and R^5 is H, or a pharmaceutically acceptable salt thereof.

22. (Original): A compound as recited in claim 1 wherein D is oxy, thio, (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is phenyl, pyridyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, isoxazolyl, pyridinazinyl, tetrazolyl, isothiazolyl, thiophenyl, furanyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyrazolyl, pyrrolyl, indolyl, naphthalenyl, quinolinyl, isoquinolinyl, benzo[b]furanyl, benzo[b]thiophenyl, benzothiazolyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, morpholinyl wherein said G is optionally mono-, di- or tri-substituted independently with halo, (C_1-C_3)alkyl or (C_1-C_3)alkoxy, or a pharmaceutically acceptable salt thereof.

23. (Original): A compound as recited in claim 22 wherein D is (C_1-C_6)alkoxy; G is phenyl, pyridyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, furanyl, 1,2,4-oxadiazolyl, 1,2,4-thiadiazolyl, pyrazolyl, pyrrolyl wherein said G is optionally mono-, di- or tri-substituted independently with halo, (C_1-C_3)alkyl or (C_1-C_3)alkoxy, or a pharmaceutically acceptable salt thereof.

24. (Original): A compound as recited in claim 1 wherein D is (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is $C(O)NR^4R^5$ or $C(S)NR^4R^5$ wherein R^4 and R^5 taken together with the nitrogen to which they are attached form a fully saturated four to nine membered ring, optionally having one to three additional heteroatoms selected independently from oxygen, sulfur and nitrogen, said ring optionally mono- or di-substituted independently with oxo, hydroxy, (C_1-C_6)alkoxy, (C_1-C_8)alkyl, amino, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or

di-N,N-(C_3-C_5)cycloalkylaminocarbonyl, N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminoor N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylamino, formylamino, (C_1-C_4) alkylformylamino, (C_3-C_5)cycloalkylformylamino, sulfamoyl, (C_1-C_4)alkylsulfonylamino, (C_3-C_5)cycloalkylsulfonylamino or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally linked through (C_1 -C_3)alkyl, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen, or a pharmaceutically acceptable salt thereof.

25. (Original): A compound as recited in claim 24 wherein D is (C_1 -C_2)alkoxy; G is C(O)NR^4R^5or C(S)NR^4R^5; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl, piperazinyl, morpholinyl, azetidinyl or pyrrolidinyl said ring optionally mono- or di-substituted independently with oxo, (C_1-C_6)alkoxy, (C_1-C_8)alkyl, amino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_3-C_5)cycloalkylaminocarbonyl, N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, mono-N- or di-N,N-(C_3-C_5)cycloalkylamino or N-(C_1-C_4)alkyl-N-(C_3-C_5)cycloalkylamino, formylamino, (C_1-C_4)alkylformylamino, (C_3-C_5)cycloalkylformylamino, sulfamoyl, (C_1-C_4)alkylsulfonylamino, (C_3-C_5)cycloalkylsulfonylamino or a partially saturated, fully saturated or fully unsaturated four to eight membered ring, optionally linked through (Ci-C_3)alkyl, optionally having one to

two heteroatoms selected independently from oxygen, sulfur and nitrogen, or a pharmaceutically acceptable salt thereof.

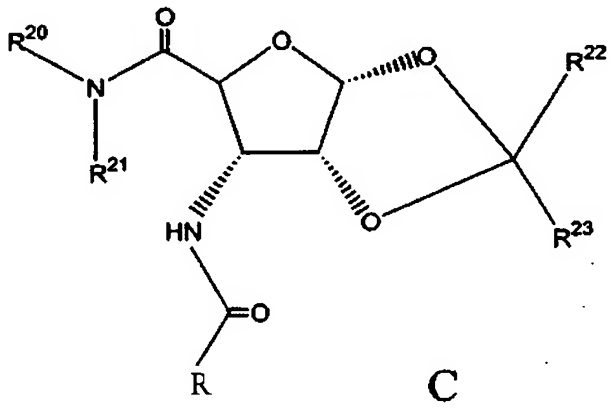
26. (Original): A compound as recited in claim 25 wherein G is $C(O)NR^4R^5$; wherein R^4 and R^5 taken together with the nitrogen to which they are attached form piperidinyl, piperazinyl, morpholinyl, azetidinyl, pyrrolidinyl said ring optionally mono- or di-substituted independently with oxo, hydroxy, (C_1-C_6)alkoxy, (C_1-C_8)alkyl, amino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylaminocarbonyl, mono-N- or di-N,N-(C_1-C_4)alkylamino, or a partially saturated, fully saturated or fully unsaturated four to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen, or a pharmaceutically acceptable salt thereof.

27. (Original): A compound as recited in claim 1 wherein D is (C_1-C_6)alkyloxy or (C_1-C_6)alkylthio; G is $C(O)NR^4R^5$ or $C(S)NR^4R^5$; R^4 is H, (C_1-C_{10})alkyl, hydroxy, (C_1-C_{10})alkoxy, (C_3-C_{10})cycloalkoxy or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through (C_1-C_3)alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally linked through (C_1-C_3)alkyl, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen; R^5 is H, (C_1-C_{10})alkyl or (C_1-C_{10})cycloalkyl, or a pharmaceutically acceptable salt thereof.

28. (Original): A compound as recited in claim 27 wherein D is $(C_1\text{-}C_2)$alkoxy; R^4 is H, $(C_1\text{-}C_{10})$alkyl, hydroxy, (C_1C_{10})alkoxy, $(C_3\text{-}C_{10})$cycloalkoxy or a partially saturated, fully saturated or fully unsaturated five to eight membered ring, optionally linked through $(C_1\text{-}C_3)$alkyl, optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen; and R^5 is H, $(C_1\text{-}C_{10})$alkyl or $(C_1\text{-}C_{10})$cycloalkyl, or a pharmaceutically acceptable salt thereof.

29. (Original): A compound as recited in claim 28 wherein G is $C(O)NR^4R^5$; R^4 is H, $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy, $(C_1\text{-}C_{10})$alkoxy or $(C_3\text{-}C_{10})$cycloalkoxy; and R^5 is H, $(C_1\text{-}C_{10})$alkyl or $(C_3\text{-}C_{10})$cycloalkyl, or a pharmaceutically acceptable salt thereof.

30. (Original): A compound having the Formula C

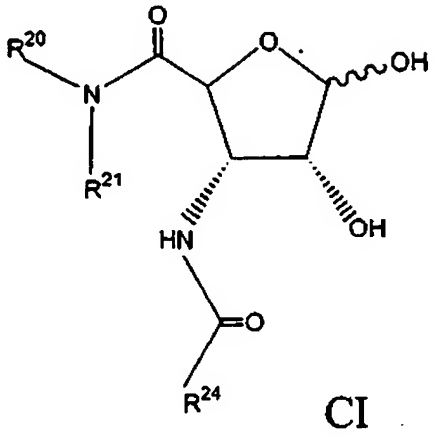


C

wherein R^{20} and R^{21} are each independently $(C_1\text{-}C_4)$alkyl, H, phenyl, phenyl$(C_1\text{-}C_4)$alkyl or are joined together to form a piperidinyl, pyrrolidinyl or morpholinyl ring; R^{22} and R^{23} are each independently $(C_1\text{-}C_4)$alkyl or are joined together to form a 5-6 membered carbocyclic ring; and R^{24} is $(C_1\text{-}C_4)$alkyl, phenyl or phenyl$(C_1\text{-}C_4)$alkyl, said phenyl or phenyl$(C_1\text{-}C_4)$alkyl

optionally mono-, di, or tri-substituted independently on the phenyl moiety with nitro, halo or trifluoromethyl.

31. (Original) A compound having the Formula CI

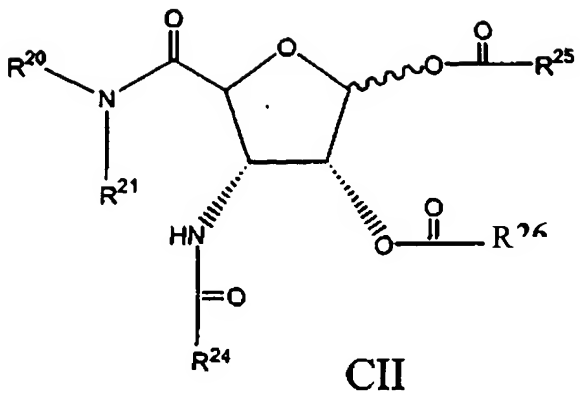


CI

wherein R^{20} and R^{21} are each independently (C_1-C_4)alkyl, H, phenyl, phenyl(C_1-C_4)alkyl or are joined together to form a piperidinyl, pyrrolidinyl or morpholinyl ring; and

R^{24} is (C_1-C_4)alkyl, phenyl or phenyl (C_1-C_4)alkyl, said phenyl or phenyl(d-d)alkyl optionally mono-, di, or tri-substituted independently on the phenyl moiety with nitro, halo or trifluoromethyl.

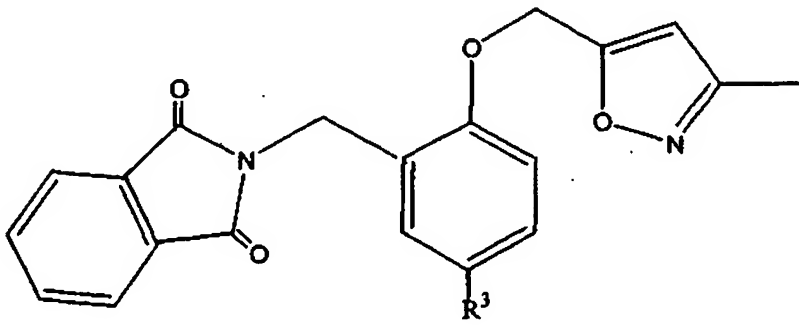
32. (Original): A compound having the Formula Cll



CII

wherein R^{20} and R^{21} are each independently (d-C_4)alkyl, H, phenyl, phenyl(d-C_4)alkyl or are joined together to form a piperidinyl, pyrrolidinyl or morpholinyl ring; R^{24} is (C_1-C_4)alkyl, phenyl or phenyl (C_1-C_4)alkyl, said phenyl or pheny(C_1-C_4)alkyl optionally mono-, di, or tri-substituted independently on the phenyl moiety with nitro, halo or trifluoromethyl; and R^{25} and R^{26} are each independently (C_1-C_4)alkyl or phenyl.

33. (Original): A compound having the Formula CIII



CIII

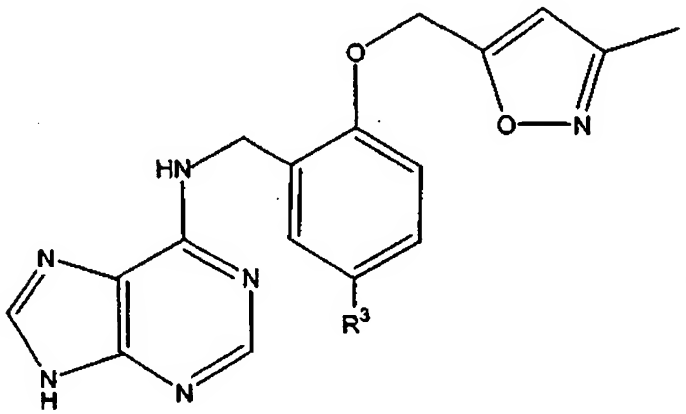
wherein R^3 is halo, trifluoromethyl, cyano, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkyloxy, ethenyl or ethynyl.

34. (Original): A compound as recited in claim 33 wherein R^3 is trifluoromethyl.

35. (Original): A compound as recited in claim 33 wherein R^3 is fluoro.

36. (Original): A compound as recited in claim 33 wherein R^3 is chloro.

37. (Original): A compound having Formula CIV



CIV

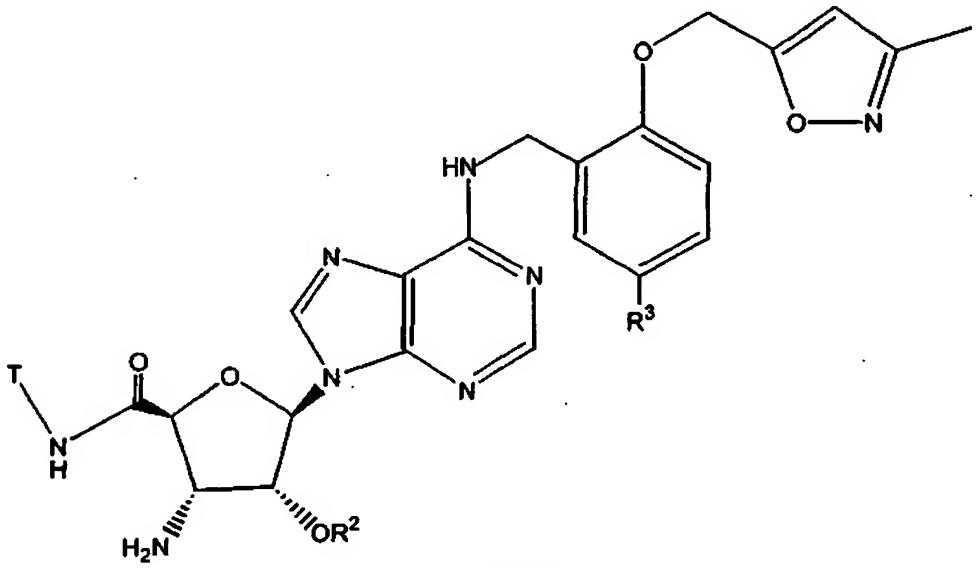
wherein R^3 is halo, trifluoromethyl, cyano, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkyloxy, ethenyl or ethynyl.

38. (Original): A compound as recited in claim 37 wherein R^3 is trifluoromethyl.

39. (Original): A compound as recited in claim 37 wherein R^3 is fluoro.

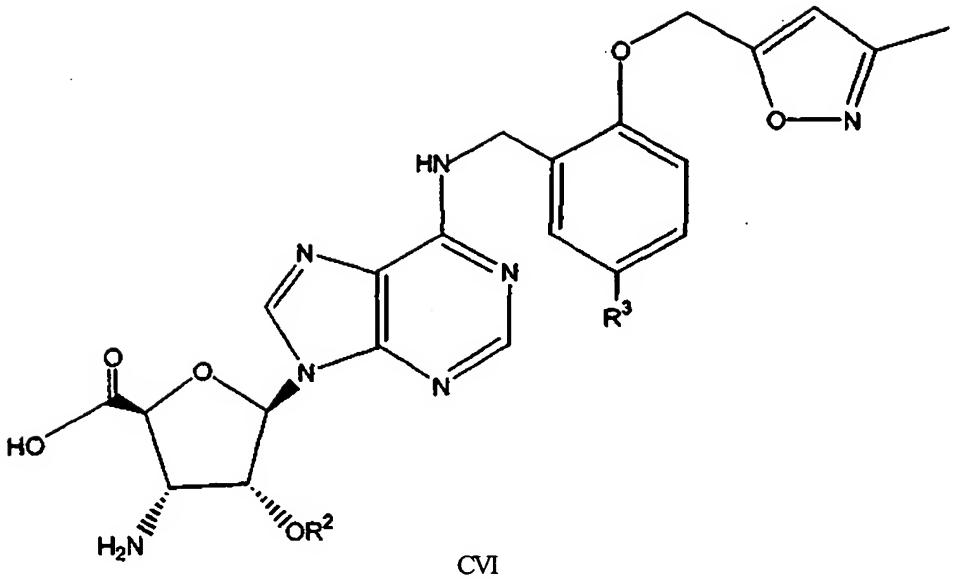
40. – 48. (Cancelled).

49. (Original): A method of making a compound of Formula CVII



CVII

wherein T is (C_1-C_4)alkyl; R^2 is H, (C_1-C_3)alkyl or (C_3-C_5)cycloalkyl; and R^3 is halo, trifluoromethyl, cyano, (C_1-C_3)alkyl, (C_1-C_3)alkyloxy, ethenyl or ethynyl; comprising acylating a (C_1-C_4)alkylamine with a Formula CVI compound



CVI

wherein R^2 is H, $(C_1\text{-}C_3)$alkyl or $(C_3\text{-}C_5)$cycloalkyl; and wherein R^3 is halo, trifluoromethyl, cyano, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkyloxy, ethenyl or ethynyl.

50. (Original): A method as recited in Claim 49 wherein R^2 is H or cyclopropyl; R^3 is fluoro, chloro or trifluoromethyl; and the Formula CVI acid is esterified to a $(C_1\text{-}C_6)$alkyl ester prior to acylation with the $(C_1\text{-}C_4)$alkylamine.

51. (Original): A method as recited in claim 50 wherein the Formula CVI acid is esterified with an alcohol in the presence of acid at a temperature of ambient to reflux for a period of about 1 hours to about 12 hours.

52. (Original): A method as recited in claim 51 wherein the ester is reacted with the amine at a temperature of about ambient to reflux for about one to about 12 hours in an alcohol solvent.

53. (Original): A method as recited in claim 52 wherein the esterification occurs at a temperature of about 50°c and the acylation occurs at a temperature of about 50°c.

54. (Original): A method as recited in claim 53 wherein the alcohol is methanol; the acid is HCI; the amine is methylamine; R^2 is H; and R^3 is chloro.

55. (Original): A method as recited in claim 53 wherein the alcohol is methanol; the acid is HCI; the amine is methylamine; R^2 is cyclopropyl; and R^3 is fluoro.

56. (Original): A method as recited in claim 53 wherein the alcohol is methanol; the acid is HCl; the amine is methylamine; R^2 is H; and R^3 is trifluoromethyl.

57. (Original): A method of reducing tissue damage resulting from ischemia or hypoxia comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1 or a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug.

58. (Original): A method as recited in claim 57 wherein the tissue is cardiac, brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal cord, retina tissue, the vasculature, or intestinal tissue.

59. (Original): A method as recited in claim 57 wherein the amount of the Formula I compound is about 0.01 mg/kg/day to about 50 mg/kg/day.

60. (Original): A method as recited in claim 59 wherein the mammal is a female or male human.

61. (Original): A method as recited in claim 60 wherein said tissue is heart tissue.

62. (Original): A method as recited in claim 60 wherein said tissue is brain tissue.

63. (Original): A method as recited in claim 60 wherein said tissue is liver tissue.

64. (Original): A method as recited in claim 60 wherein said tissue is kidney tissue.

65. (Original): A method as recited in claim 60 wherein said tissue is lung tissue.

66. (Original): A method as recited in claim 60 wherein said tissue is gut tissue.

67. (Original): A method as recited in claim 60 wherein said tissue is skeletal muscle tissue.

68. (Original): A method as recited in claim 60 wherein said tissue is spleen tissue.

69. (Original): A method as recited in claim 60 wherein said tissue is pancreas tissue.

70. (Original): A method as recited in claim 60 wherein said tissue is retina tissue.

71. (Original): A method as recited in claim 60 wherein the compound is administered prophylactically.

72. (Original) A method as recited in claim 60 wherein the compound is administered prior to surgery.

73. (Original): A method as recited in claim 60 wherein the compound is administered prior to cardiac surgery.

74. (Original) A method as recited in claim 60 wherein the compound is administered prior to, during and after surgery.

75. (Original) A method as recited in claim 60 wherein the compound is administered prior to, during and after cardiac surgery.

76. (Original) A method as recited in claim 60 wherein the compound is administered within twenty-four hours after surgery.

77. (Original) A method as recited in claim 60 wherein the compound is administered within twenty four hours after cardiac surgery.

78. (Original) A method as recited in claim 60 wherein the tissue damage resulting from ischemia or hypoxia is ischemic or hypoxic damage and is incurred during organ transplantation.

79. (Original) A method as recited in claim 60 wherein the compound is administered to prevent perioperative myocardial ischemic injury.

80. (Original) A pharmaceutical composition which comprises a therapeutically effective amount of a compound of claim 1 or a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug and a pharmaceutically acceptable carrier, vehicle or diluent.

81. (Original) A pharmaceutical composition for the reduction of tissue damage resulting from ischemia or hypoxia which comprises a therapeutically effective amount of a compound of

claim 1 or a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug and a pharmaceutically acceptable carrier, vehicle or diluent.

82. (Original) A pharmaceutical combination composition comprising: a therapeutically effective amount of a composition comprising a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; a second compound, said second compound being an aldose reductase inhibitor; and a pharmaceutical carrier, vehicle or diluent.

83. (Original) A pharmaceutical composition as recited in claim 82 wherein the aldose reductase inhibitor is 1-phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[[5-trifluoromethyl)-2-benzothiazolyl]methyl]- or a pharmaceutically acceptable salt thereof.

84. (Original) A method of reducing tissue damage resulting from ischemia or hypoxia comprising administering to a mammal in need of such treatment an amount of a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; an amount of a second compound, said second compound being an aldose reductase inhibitor; wherein the amounts of the first and second compounds result in a therapeutic effect.

85. (Original) A method of reducing tissue damage resulting from ischemia or hypoxia as recited in claim 84 wherein the aldose reductase inhibitor is 1-phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[[5-trifluoromethyl)-2-benzothiazolyl]methyl]- or a pharmaceutically acceptable salt thereof.

86. (Original): A kit comprising: a first compound, said first compound being a compound of claim 1 , a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug and a pharmaceutically acceptable carrier, vehicle or diluent in a first unit dosage form; b. a second compound, said second compound being an aldose reductase inhibitor and a pharmaceutically acceptable carrier, vehicle or diluent in a second unit dosage form; and c. means for containing said first and second dosage forms wherein the amounts of first and second compounds result in a therapeutic effect.

87. (Original): A kit as recited in claim 86 wherein the aldose reductase inhibitor is 1-phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[[5-trifluoromethyl)-2-benzothiazolyljmethyl]- or a pharmaceutically acceptable salt thereof.

88. (Original): A pharmaceutical combination composition comprising: a therapeutically effective amount of a composition comprising a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; a second compound, said second compound being a glycogen phosphorylase inhibitor; and a pharmaceutical carrier, vehicle or diluent.

89. (Original): A pharmaceutical composition as recited in claim 88 wherein the glycogen phosphorylase inhibitor is 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl-(2R)-hydroxy-3-((3S)-hydroxypyrrolidin-1-yl)-3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((3S,4S)-dihydroxypyrrolidin-1-yl) -(2R)-hydroxy- 3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl]-

amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-methoxy-methyl-carbamoyl)-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxyimino-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethy!]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((cis)-dihydroxypyrrolidin-1-yl) -(2R)-hydroxy- 3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-((3S,4S)-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(1,1-dioxo-thiazolidin-3-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1 S)-(4-fluoro-benzyl)-2-(4-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1 S)-benzyl-2-((3RS)-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-oxo-2-((1 RS)-oxo-thiazolidin-3-yl)-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxy-azetidin-1-yl)-2-oxo-ethyl]-amide; or a pharmaceutically acceptable salt thereof.

90. (Original) A method of reducing tissue damage resulting from ischemia or hypoxia comprising administering to a mammal in need of such treatment an amount of a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; and an amount of a second compound, said second compound being a glycogen phosphorylase inhibitor; wherein the amounts of first and second compounds result in a therapeutic effect.

91. (Original): A method of reducing tissue damage resulting from ischemia as recited in claim 90 wherein the glycogen phosphorylase inhibitor is 5-chloro-lH-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3S)-hydroxypyrrolidin-1-yl)-3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((3S,4S)-dihydroxypyrrolidin-1-yl) -(2R)-hydroxy- 3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-methoxy-methyl-carbamoyl)-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxyimino-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((cis)-dihydroxypyrrolidin-1yl)-(2R)-hydroxy- 3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-((3S,4S)- dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1 S)-benzyl-2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(1,1-dioxo-thiazolidin-3-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-(4-fluoro-benzyl)-2-(4-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-((3RS)-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-oxo-2-((1 RS)-oxo-thiazolidin-3-yl)-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxy-azetidin-1-yl)-2-oxo-ethyl]-amide; or a pharmaceutically acceptable salt thereof.

92. (Original): A kit comprising: a. a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug and a

pharmaceutically acceptable carrier, vehicle or diluent in a first unit dosage form; b. a second compound, said second compound being an glycogen phosphorylase inhibitor and a pharmaceutically acceptable carrier, vehicle or diluent in a second unit dosage form; and c. means for containing said first and second dosage forms wherein the amounts of first and second compounds result in a therapeutic effect.

93. (Original): A kit as recited in claim 92 wherein the glycogen phosphorylase inhibitor is 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3S)-hydroxypyrrolidin-1-yl)-3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((3S,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy- 3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl]-amide; -chloro-1H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-methoxy-methyl-carbamoyl)-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1 H-indole-2-carboxylic acid [(1S)- ((R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl)-2-phenyl-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxyimino-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(IS)-benzyl -3-((cis)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxopropyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-((3S,4S)- dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1 S)-benzyl-2-(cis-3,4-dihydroxy-pyrrolidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-(1,1-dioxo-thiazolidin-3-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1 S)-(4-fluoro-benzyl)-2-(4-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-((3RS)-hydroxy-piperidin-1-yl)-2-oxo-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [2-oxo-2-((1RS)-oxo-thiazolidin-3-yl)-ethyl]-amide; 5-chloro-1H-indole-2-

carboxylic acid [2-oxo-2-((1RS)-oxo-thiazolidin-3-yl)-ethyl]-amide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-2-(3-hydroxy-azetidin-1-yl)-2-oxo-ethyl]-amide; or a pharmaceutically acceptable salt thereof.

94. (Original): A pharmaceutical combination composition comprising: a therapeutically effective amount of a composition comprising a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; a second compound, said second compound being a cardiovascular agent; and a pharmaceutical carrier, vehicle or diluent.

95. (Original): A pharmaceutical composition as recited in claim 94 wherein the cardiovascular agent is a p-blocker, a calcium channel blocker, a potassium channel opener, adenosine, adenosine agonists, an ACE inhibitor, a nitrate, a diuretic, a glycoside, a thrombolytic, a platelet inhibitor, aspirin, dipyridamol, potassium chloride, clonidine, prazosin, pyruvate dehydrogenase kinase inhibitors, pyruvate dehydrogenase complex activators, biguanides, NHE-1 inhibitor, Angiotensin II (All) receptor antagonists, C5a inhibitors, soluble complement receptor type 1 (sCR1) or analogues, partial fatty acid oxidation (PFOX) inhibitors (specifically, ranolazine), acetyl CoA carboxylase activators, malonyl CoA decarboxylase inhibitors, 5'AMP-activated protein kinase (AMPK) inhibitors, adenosine nucleoside inhibitors, anti-apoptotic agents (e.g., caspase inhibitors), monophosphoryl lipid A or analogues, nitric oxide synthase activators/inhibitors, protein kinase C activators (specifically, protein kinase ε), poly (ADP ribose) synthetase (PARS, PARP) inhibitors, metformin (gluconegenesis inhibitors, insulin

sensitizers), endothelin coverting enzyme (ECE) inhibitors, endothelin ETA receptor antagonists, TAFI inhibitors, or a Na/Ca exchanger modulators.

96. (Original): A pharmaceutical composition as recited in claim 95 wherein the NHE-1 inhibitor is [1-(8-bromoquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(6-chloroquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(indazol-7-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(benzimidazol-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(1-isoquinolyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [5-cydopropyl-1-(4-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine; [5-cyclopropyl-1-(quinolin-5-yl)-1H-pyrazole-4-carbonyl]guanidine; [5-cyclopropyl-1-(quinolin-8-yl)-1H-pyrazole-4-carbonyl]guanidine; [1-(indazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(indazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(benzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(1-methylbenzimidazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; 1 -(5-quinolinyl)-5-n-propyl-1H-pyrazole-4-carbonyl]guanidine; [1-(5-quinolinyl)-5-isopropyl-1H-pyrazole-4-carbonyl]guanidine; [5-ethyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine; [1-(2-methylbenzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(1,4-benzodioxan-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(benzotriazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1-(3-chloroindazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine; [1 -(5-quinolinyl)-5-butyl-1H-pyrazole-4-carbonyl]guanidine; [5-propyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine; [5-

isopropyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-4-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-trifluoromethyl-4-fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-bromophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1 -(2-chloro-5-methoxyphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-4-methylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2,5-dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2,3-dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-5-aminocarbonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-5-aminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyljguanidine; [1-(2-fluoro-6-trifluoromethylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-5-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chloro-5-dimethylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-trifluoromethyl-4-chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine; [1-(2-chlorophenyl)-5-methyl-1H-pyrazole-4-carbonyl]guanidine; [5-methyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine; [5-ethyl-1-phenyl-1H-pyrazole-4-carbonyl]guanidine; [5-cyclopropyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine; [5-cyclopropyl-1-phenyl-1 H-pyrazole-4-carbonyl]guanidine; [5-cyclopropyl-1-(2,6-dichlorophenyl)-1H-pyrazole-4-carbonyl]guanidine or the pharmaceutically acceptable salts of said compounds.

97. (Original): A method of reducing tissue damage resulting from ischemia or hypoxia comprising administering to a mammal in need of such treatment an amount of a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said prodrug; an amount of a second compound, said second compound being a cardiovascular agent; wherein the amounts the of first and second compounds result in a therapeutic effect.

98. (Original): A method of reducing tissue damage resulting from ischemia or hypoxia as recited in claim 97 wherein the cardiovascular agent is a (3-blocker, a potassium channel opener, adenosine, adenosine agonists, a calcium channel blocker, an ACE inhibitor, a nitrate, a diuretic, a glycoside, a chrombolytic, a platelet inhibitor, aspirin, dipyridamol, potassium chloride, clonidine, prazosin, pyruvate dehydrogenase kinase inhibitors, pyruvate dehydrogenase complex activators, biguanides, NHE-1 inhibitor, Angiotensin II (All) receptor antagonists, C5a inhibitors, soluble complement receptor type 1 (sCR1) or analogues, partial fatty acid oxidation (PFOX) inhibitors (specifically, ranolazine), acetyl CoA carboxylase activators, malonyl CoA decarboxylase inhibitors, 5'AMP-activated protein kinase (AMPK) inhibitors, adenosine nucleoside inhibitors, anti-apoptotic agents (e.g., caspase inhibitors), monophosphoryl lipid A or analogues, nitric oxide synthase activators/inhibitors, protein kinase C activators (specifically, protein kinase ε), poly (ADP ribose) synthetase (PARS, PARP) inhibitors, metformin (gluconegenesis inhibitors, insulin sensitizers), endothelin coverting enzyme (ECE) inhibitors, endothelin ET A receptor antagonists, TAFI inhibitors, or a Na/Ca exchanger modulators.

99. (Original): A kit comprising: a. a first compound, said first compound being a compound of claim 1, a prodrug thereof, or a pharmaceutically acceptable salt of said compound or of said

prodrug and a pharmaceutically acceptable carrier, vehicle or diluent in a first unit dosage form; b. a second compound, said second compound being a cardiovascular agent and a pharmaceutically acceptable carrier, vehicle or diluent in a second unit dosage form; and c. means for containing said first and second dosage forms wherein the amounts of the first and second compounds result in a therapeutic effect.

100. (Original): A kit as recited in claim 99 wherein the cardiovascular agent is a P-blocker, a calcium channel blocker, an ACE inhibitor, a nitrate, a diuretic, a glycoside, a thrombolytic, a platelet inhibitor, aspirin, dipyridamol, potassium chloride, clonidine, prazosin, pyruvate dehydrogenase kinase inhibitors, pyruvate dehydrogenase complex activators, biguanides or an NHE-1 inhibitor.

101. (Original): A compound selected from the group consisting of (2S,3S,4R,5R)3-Amino-5-[6-(2-benzyloxy-5-chloro-benzylamino)-purin-9-yl]-4-hydroxytetrahydrofuran-2-carboxylic acid methylamide, (2S,3S,4R,5R)3-Amino-5-{6-[5-chloro-2-(furan-3-ylmethoxy)benzylamino]-purin-9-yl}-4-hydroxytetrahydrofuran-2-carboxylic acid methylamide, (2S,3S,4R,5R)3-Amino-5-{6-[5-chloro-2-(furan-2-ylmethoxy)benzylamino] purin-9-yl}-4-hydroxytetrahydrofuran-2-carboxylic acid methylamide, (2S,3S,4R,5R)3-Amino-5-{6-[5-chloro-2-(thiazol-2-ylmethoxy)-benzylamino]-purin-9-yl}-4-hydroxy-tetrahydro-furan-2-carboxylicacid methylamide, (2S,3S,4R,5R)3-Amino-5-{6-[5-chloro-2-(3-methylisoxazol-5-ylmethoxy) benzylamino]purin-9-yl}-4-hydroxytetrahydrofuran-2- carboxylic acid methylamide or the pharmaceutically acceptable salts of said compounds.